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Evaluation of platelet and white cell parameters among pregnant women with Preeclampsia in Gondar, Northwest Ethiopia: A comparative cross-sectional study

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ABSTRACT

Objective: To evaluate platelet and White cell parameters in women with preeclampsia (PE) in comparison with a healthy pregnancy.
Methods: A cross-sectional study was carried in 2015 at University of Gondar hospital. Thirty-three mild PE, 30 severe PE cases and 63 healthy pregnant women were enrolled in the study. About 3 mL venous blood sample was collected from each study participants. Hematological parameters were determined by Sysmex KX-21 hematological analyzer. Data normality was checked by Kolmogorov-Smirnov normality test. One way analysis of variance with Bonferroni test and Pearson's product moment correlation were done for normally distributed data. For non-normally distributed data, Kruskal-Wallis H test with the Mann-Whitney *U* test and Spearman's rank-order Correlation test were done using SPSS 20.0 for Windows. A p-value < 0.05 was considered as statistically significant.
Results: The means of white blood cells (WBC), absolute Neutrophil count (ANC), Absolute middle cell count (AMC), mean Platelet count (PTC), Platelet distribution width (PDW), neutrophil-to-lymphocyte ratio (NLR), and median of platelet-to-large cell ratio (P-LCR) were significantly increased; while Absolute lymphocyte count (ALC) and platelet count (PTC) were significantly decreased in PE groups. WBC, ANC, MPV, PDW, P-LCR and NLR showed statistically significant positive correlations, whereas PTC displayed a statistically significant negative correlation with a MAP in PE group.
Conclusion: WBC, ANC, MPV, PDW, P-LCR and NLR were increased as PE advanced. PTC decreased with the severity of the disease. Evaluation of these parameters as a supportive clinical marker in the assessment of severity may assist the management of PE.

1. Introduction

Preeclampsia (PE), which is a pregnancy-specific multi-systemic disorder, is a leading cause of morbidity and mortality for both mothers and fetus [1]. It affects 5–8% of all pregnancies and contributing to 50,000–60,000 annual maternal death globally [2]. In Ethiopia, about 54,000 up to 216,000 women are estimated to develop PE, and it is responsible for 11% of all death of a mother and 16% of all direct maternal death [3]. PE is characterized by the new development of hypertension and proteinuria at ≥20 weeks of pregnancy [1]. Without proteinuria, it can be diagnosed by hypertension along with other diagnostic criteria [4].

Even though the aetiology and pathogenesis of PE continue to be enigmatic, an exaggerated intravascular inflammatory response to

Abbreviations: ALC, Absolute Lymphocyte Count; AMC, Absolute Middle cells Count; ANC, Absolute Neutrophil Count; ANOVA, Analysis of Variance; DBP, Diastolic Blood Pressure; IQR, Interquartile Range; MAP, Mean Arterial Pressure; MPV, Mean Platelet Volume; MXD, Middle cells; NLR, Neutrophil-to-Lymphocyte ratio; PDW, Platelet Distribution Width; PE, Preeclampsia; PLC, Percentage Lymphocyte Count; P-LCR, Platelet-Large Cell Ratio; PLR, Platelet-to-Lymphocyte Ratio; PMC, Percentage Middle cells Count; PNC, Percentage Neutrophil Count; PTC, Platelet Count; SBP, Systolic Blood Pressure; SD, Standard Deviation; WBC, White Blood Cells

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pregnancy is considered to be the major role player of PE [5,6]. Activations of platelets, leukocyte and systemic endothelial activation are exaggerated in PE compared to normal pregnancy; and their interaction supposed to result in the vascular damage in PE [7,8]. It has been documented that leukocyte activation plays an important role in the pathogenesis of PE [8]. A recent study revealed that the interactions of platelets with different cell types (endothelial, dendritic, T-lymphocytes, neutrophils and mononuclear phagocytes) can trigger and exaggerate the inflammation in the arterial wall [9]. Thus, platelets may involve in promoting an inflammatory response in PE through their interaction with leukocytes and endothelium as crucial inflammatory role players [2]. Endothelial dysfunction predates the beginning of symptomatic clinical manifestations, which appears to be caused by the exaggerated systemic inflammatory response. The central nervous system, lung, liver, kidney, systemic vasculature, coagulation, heart, placenta and fetus are subjected to exacerbated inflammation and endothelial injury [10].

As its aetiology and pathogenesis remain unclear, there are no specific preventive and treatment choices [11]. Delivery of fetus and placenta are being described as the sole effective treatment for PE [12]. Likewise, there are no clinical and laboratory-based models to predict the occurrence of PE as well as the likelihood of detrimental outcomes for mothers presenting with uncomplicated PE [13]. Still now, there is a continuous search for effective tools to predict the development and severity of disease [14]. As stated by the International Society for the Study of Hypertension in Pregnancy, the degree of proteinuria is excluded from the diagnostic criterion for assessment of severity of PE because of its lesser value for further risk identification though it assists the diagnosis of PE. Accordingly, the hematological parameters and the ratio of classes of blood cell (Platelet-to-Lymphocyte ratio(PLR) and the Neutrophil-to-Lymphocyte ratio(NLR)), which have been recently applied to be systemic inflammatory response markers [15], could be options for clinical evaluation of adverse maternal and fetal outcomes in PE.

In PE, evaluating the changes in hematological parameters is essential to prevent both maternal and fetal morbidity and mortality. Estimating the variations in hematological parameters in PE compared with a healthy pregnancy, and their relation with severity of disease has paramount importance in assessing disease progression and managing related complications. However, there is no much-published data describing hematological parameters with a degree of severity of PE in Ethiopia. Therefore, this study was designed to assess changes in white cell and platelet parameters in PE compared to healthy pregnancy, and their relation with severity of the disease.

2. Methods and materials

2.1. Study design, setting and period

An institutional based cross-sectional analytical study was carried out among pregnant women with PE attending antenatal care clinic and admitted at the maternity ward, and healthy pregnant women who were attending antenatal care service at antenatal care clinic, University of Gondar Referral Hospital. The hospital is found in Gondar town, northwest Ethiopia. It is at 727 km far away from Addis Ababa, the capital city of Ethiopia. The hospital gives service to about 6 million people. The study was done from February–August 2015.

2.2. Sample size and sampling technique

According to rules of thumb that have been recommended by van Voorhis and Morgan, 30 participants per group are required to detect real differences, which could lead to about 80% power [16]. Accordingly, 126 study subjects (33 with mild PE, 30 with severe PE and 63 with healthy pregnancy as a control) were recruited into this study. Healthy pregnant women voluntarily participated in the study and were taken from study population by convenience i.e. sequential sampling technique.

2.3. Source and study population

All pregnant women who had a follow-up care and pregnant women with PE admitted at University of Gondar hospital maternity ward were the source population. The study population were women with PE at > 20 weeks of gestation, and healthy pregnant women who were matched for the age and gestational weeks.

2.4. Inclusion and exclusion criteria

Pregnant women with PE at > 20 weeks of gestation, and age and gestational age-matched normotensive women with uncomplicated pregnancy were included in the study. Pregnant women who had a history of smoking, epilepsy, hypertension, diabetes mellitus, chronic systemic disease and chronic inflammatory disorders prior to pregnant state; and those infected with clinically diagnosed infectious diseases were excluded from the study. Pregnant women having ruptured membranes, taking an anti-inflammatory (corticosteroids or non-steroidal) and anticoagulants medication, and multiple pregnancies were also excluded.

2.5. Operational definitions

Definition and classification of PE were based on the recommendation of the American College of Obstetricians and Gynecologists task force on hypertension in Pregnancy [4]. PE is defined as systolic blood pressure (SBP) ≥140 and/or a diastolic blood pressure (DBP) ≥90 mmHg on two measurements together with proteinuria of ≥1 + by dipstick in a random urine sample after 20 weeks of pregnancy. PE is taken as mild if SBP/DBP is ≥140/90 mmHg and proteinuria of ≥1 + or more using dipstick after the 20 weeks of gestation in the absence of severe PE criteria. PE is considered as severe if it presented with one or more of the following criteria: SBP ≥160 mmHg or DBP ≥110 mmHg or both, new-onset cerebral or visual disturbance, epigastric or right upper quadrant pain, pulmonary oedema, and new onset seizures.

3. Data collection and laboratory methods

3.1. Socio-demographic and clinical data collection

Socio-demographic, family, medical and obstetric history data were obtained by medical record review and face-to-face interview. Study participants were interviewed with a structured questionnaire. Blood pressure readings of study participants s were measured and recorded using mercury sphygmomanometer according to the recommendation of Hypertension Guideline Committee [17]. As a marker of PE severity, mean arterial pressure (MAP) was calculated as DBP plus 1/3 of the difference between SBP and DBP

3.2. Laboratory analysis

Fresh urine specimens were collected in a clean dry container. Proteinuria was determined by Cromatest® Linear URS-10 strips (Linear Chemicals S.L, 08390 Montgat (Barcelona), Spain). Three ml venous blood sample was collected into vacutainer tube with an ethylene-diaminetetra-acetic acid anticoagulant. Hematological parameters were determined by Sysmex KX-21(Sysmex Corporation, Kobe, Japan) automated hematology analyzer within 1-h blood sample collection. All procedures were conducted according to the manufacturers' instruction manual.

3.3. Ethical consideration

Before commencement of the study, the study was ethically approved by School of Biomedical and Laboratory Sciences Research and Ethical Committee (Reference number: SBMLS/927/07). Permission letter was obtained from the administrator of University of Gondar hospital. Each study participants were requested to participate voluntarily. Written informed consent was obtained from each study participants. Voluntary participation and the right to withdraw were assured for each participant. Privacy and confidentiality were maintained during and/or after the interview. The laboratory results were communicated to the authorized clinicians.

3.4. Data analysis and interpretation

Data were coded and cleaned before data analysis. Data analysis was performed using SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov normality test was run for checking the distribution of hematological parameters and the Levene statistic test was used to test the homogeneity of variances. One way analysis of variance test and Bonferroni pairwise comparison tests were conducted for comparison of normally distributed variables. The results of normally distributed variables are presented as the mean ± standard deviation (SD). Kruskal-Wallis H test in conjunction with the Mann-Whitney *U* test was used for comparison of non-normally distrusted hematological parameters, and the results are presented as median and Interquartile Range (IQR). For the evaluation of the correlations of parameters with a MAP, Spearman's rank-order Correlation test was used. A p-value < 0.05 was considered as statistically significant for all analyses. The results of the study were summarized using tables and texts.

4. Results

4.1. Characteristics of study participants

The median [IQR] age of the control and PE group was 26.00[6.00] and 25.00[8.00] years, respectively. In this study, no statistically significant differences between the control and PE groups in age, number of pregnancies (gravidity), number of deliveries (parity) and gestational weeks were observed as outlined in Table 1.

4.2. White cell parameters

The mean (± SD) WBC, ANC and NLR have shown significant elevation in women with PE as compared to control group. But ALC was significantly decreased in PE group than the control group. The median [IQR] AMC (Middle cells: basophils, eosinophils and monocytes) has shown significant elevation in PE group as compared to the control group ($P < 0.001$) (Table 2).

In Bonferroni pairwise comparison tests between groups, there were statistically significant differences between the three groups of the study population with regard to the mean WBC, ANC and NLR, which were significantly increased with the severity of PE ($p < 0.05$). However, no significant difference was found between mild and severe PE ($p = 0.65$), while a significant difference was observed between mild PE and the control group ($p = 0.044$), and severe PE and the control group ($p = 0.043$) for mean ALC. In Mann-Whitney *U* test pairwise comparisons, there was no a significant difference between mild and severe PE ($p = 0.109$), while significant difference was detected between mild PE and the control group ($P = 0.007$) and severe PE and the control group ($P < 0.001$) in median(IQR) AMC value (Table 3).

Table 1
Characteristics of healthy pregnant women and preeclamptic women participated in the study (n = 126).

Characteristics	Healthy pregnancy (median[IQR]) (n = 63)	PE (median[IQR]) (n = 63)	P-value
Age (in years)	26.00[6.00]	25.00[8.00]	0.319
Number of pregnancy	2.00[2.00]	1.00[1.00]	0.257
Number of delivery	1.00[1.00]	1.00[1.00]	0.120
Gestational age (in weeks)	37.00[4.50]	37.60[3.80]	0.075
SBP (mmHg)	110.00[10.00]	150.00[10.00]	< 0.001
DBP (mmHg)	70.00[15.00]	100.00[10.00]	< 0.001
MAP (mm Hg)	83.33[11.67]	120.00[6.67]	< 0.001

4.3. Platelet parameters

As presented in Table 4, the mean ± SD platelet count (PTC) was significantly lower in PE group (158.38 ± 42.71 × 10^3/μL) compared to the control group (194.05 ± 45.59 × 10^3/μL). Whereas mean platelet volume (MPV) and platelet distribution width (PDW) were significantly higher in PE group (11.28 ± 0.97 fL and 16.06 ± 2.44 fL, respectively) than the control group (10.31 ± 1.13 fL and 14.01 ± 2.54 fL, respectively) in ANOVA test. In Mann-Whitney *U* test, median [IQR] platelet large cell ratio (P-LCR) level was also significantly higher in PE (35.00[10.20]%) than the control group (27.00[11.10] %).

In Bonferroni pairwise comparison tests between groups, there were statistically significant differences among the control, mild and severe PE groups with regard to PTC which showed a declining value with the severity of disease, whereas MPV and PDW significantly increased with the severity of PE. Moreover, the mean value of P-LCR has shown a significant elevation in severe PE group compared to the control group. In Kruskal-Wallis H test and Mann-Whitney *U* test pairwise comparisons, the median P-LCR has shown significant differences among the three groups; significantly elevated as the disease severity advances (Table 5).

4.4. Correlation analysis

For assessment of the association of hematological parameters with the severity of disease, their correlation with the MAP was computed in mild and severe PE groups for those parameters that showed significant differences between PE groups. In correlation analysis, a MAP showed statistically significant positive correlations with WBC (rho = 0.52), ANC (rho = 0.51), MPV (rho = 0.37), PDW (rho = 0.43), P-LCR (rho = 0.44) and NLR (rho = 0.31) in PE group. Similarly, it showed statistically significant negative correlation with PTC (rho = −0.33) (Table 6).

5. Discussion

PE is one of the commonest grave complications of pregnancy [18] and a significant health problem, which needs a due attention particularly in developing nations where the risk of adverse outcomes are high [19]. The aetiology and pathogenesis of PE continue to be blurred in the face of exhaustive research efforts [5]. However, extensive systemic maternal inflammatory response and endothelial cell dysfunction recently have been proposed to be critical players [18]. Currently, there are no available tests for the clinical diagnosis of PE based on tests that drown from its' etiopathogenesis [1]. Likewise, there is no laboratory method to assess the likelihood of detrimental outcomes for mothers presenting with uncomplicated PE. This study was performed to evaluate white blood cell and platelet parameters as well as the two derived parameters, NLR and PLR, based on the information that PE is an inflammatory disease.

In this study, we observed statistically significant elevated leukocyte and neutrophil count in PE group as compared to the control group (p-

Table 2
Comparisons of total and differential WBC count between healthy pregnant and preeclamptic women.

WBC parameters	Healthy pregnancy (n = 63)	PE (n = 63)	P value
Total WBC ($\times 10^3/\mu L$)©	8.18 ± 2.05	10.71 ± 3.49	< 0.001
Absolute neutrophil count (ANC)($\times 10^3/\mu L$)©	5.56 ± 1.54	7.92 ± 2.86	< 0.001
Absolute lymphocyte count (ALC)($\times 10^3/\mu L$)©	1.92 ± 0.45	1.70 ± 0.32	0.003
Absolute middle cells count (AMC)($\times 10^3/\mu L$)©	0.70[0.30]	1.00[0.70]	< 0.001
Percentage neutrophil count (PNC) (%)©	67.64 ± 3.68	73.27 ± 4.04	< 0.001
Percentage lymphocyte count (PLC) (%)©	23.61 ± 3.25	16.93 ± 4.15	< 0.001
Percentage mixed count (PMC) (%)*	8.20[2.50]	9.80[2.70]	0.002
Neutrophil-to-lymphocyte ratio (NLR)©	2.92 ± 0.50	4.67 ± 1.50	< 0.001

© Data were expressed as Mean ± SD.
* Data were expressed as Median(IQR).

Table 3
Comparisons of total and differential WBC count between women healthy pregnancy, mild PE and severe PE.

WBC parameters	Healthy Pregnancy (n = 63)	Mild PE (n = 33)	Severe PE (n = 30)	¤P value	*P value	**P Value	***P value
Total WBC ($\times 10^3/\mu L$)©	8.18 ± 2.05	9.84 ± 3.22	11.66 ± 3.57	< 0.001	< 0.001	0.02	0.033
ANC ($\times 10^3/\mu L$)©	5.56 ± 1.54	7.12 ± 2.47	8.81 ± 3.02	< 0.001	< 0.001	0.004	0.009
ALC ($\times 10^3/\mu L$)©	1.92 ± 0.45	1.71 ± 0.37	1.70 ± 0.28	0.012	0.044	0.043	0.65
AMC ($\times 10^3/\mu L$)*	0.70(0.30)	0.90(0.75)	1.10(0.62)	< 0.001	< 0.001	0.007	0.109
PNC (%)©	67.64 ± 3.68	72.14 ± 3.55	74.52 ± 4.24	< 0.001	< 0.001	< 0.001	0.043
PLC (%)©	23.61 ± 3.25	18.09 ± 3.88	15.66 ± 4.13	< 0.001	< 0.001	< 0.001	0.057
PMC (%)*	8.20[2.50]	9.80[4.25]	9.85[2.23]	0.006	0.003	0.03	0.951
NLR©	2.92 ± 0.50	4.05 ± 1.13	5.21 ± 1.68	< 0.001	< 0.001	< 0.001	< 0.001

*P value of comparison of severe PE and healthy pregnancy in a pairwise comparison test.
**P value of comparison of mild PE to healthy pregnancy in a pairwise comparison test.
***P value of comparison of severe PE to mild PE in a pairwise comparison test.
PNC: percentage of a neutrophil count; PLC: percentage of lymphocyte count; PMC: percentage of middle cell count.
¤ P value of comparison among healthy pregnancy, mild PE and severe PE groups.
© Data were expressed as Mean ± SD.
* Data were expressed as Median[IQR].

Table 4
Comparisons of platelet parameters between healthy pregnant and pre-eclamptic women.

Platelet parameters	Healthy Pregnancy (n = 63)	PE (n = 63)	P value
PTC($\times 10^3/\mu L$)©	194.05 ± 45.59	158.38 ± 42.71	< 0.001
MPV(fL)©	10.31 ± 1.13	11.28 ± 0.97	< 0.001
PDW(fL)©	14.01 ± 2.54	16.06 ± 2.44	< 0.001
P-LCR (%)*	27.00[11.10]	35.00[10.20]	< 0.001
Platelet-to-lymphocyte ratio(PLR) ©	108.08 ± 40.30	96.94 ± 33.96	0.097

© Data were expressed as Mean ± SD.
* Data were expressed as median(IQR).

value < 0.05). Similar findings have been reported by Alisi P. Nc et al [20], Ghosh et al [21], Mihu et al [22], and Ünlü1 et al [6]. Our study is also in consonance with the study that corroborates an exaggerated inflammatory response in PE than healthy pregnancy [7]. Tough it was not statistically significant, Ceyhan et al. reported that the mean WBC count was higher in PE compared to the control group [23]. In the above study, small numbers of study subjects relative to our sample size were enrolled. This could be the probable explanation for the observed discrepancy between Ceyhan et al and our finding. Our observation in the neutrophil count is similar to report of Alisi et al who observed a statistically significant increase in women with PE compared with the control group [20]. Neutrophil count in the present study is also consistent with the results of previous studies [21,22]. Moreover, statistically significant higher ANC has been reported by Canzoneri et al [8] who proposed that leukocytosis noticed in PE would be as a result of increment in the number of neutrophils.

Statistically significant changes in WBC and neutrophil counts were also observed when PE groups were compared with each other and with the control group. Our result is in agreement with previous studies which demonstrated that increased values in severe PE compared to the

Table 5
Pairwise Comparisons of platelet parameters among women with healthy pregnancy, mild and severe preeclampsia.

Platelet parameters	Healthy pregnancy (n = 63)	Mild PE (n = 33)	Severe PE (n = 30)	¤P value	*P value	**P value	***P value
PTC($\times 103/\mu L$)©	194.05 ± 45.59	171.06 ± 36.91	144.43 ± 44.86	< 0.001	< 0.001	0.045	0.049
MPV(fL)©	10.31 ± 1.13	10.97 ± 1.13	11.61 ± 0.63	< 0.001	< 0.001	0.011	0.045
PDW(fL)©	14.01 ± 2.54	15.30 ± 2.54	16.90 ± 2.07	< 0.001	< 0.001	0.045	0.032
P-LCR (%)*	27.00[11.10]	33.30[11.10]	37.50[8.18]	< 0.001	< 0.001	0.007	< 0.001
PLR©	108.08 ± 40.30	102.50 ± 33.54	87.67 ± 32.45	0.04	0.042	0.69	0.175

*P value of comparison of severe PE and healthy pregnancy in a pairwise comparison test.
**P value of comparison of mild PE to healthy pregnancy in a pairwise comparison test.
***P value of comparison of severe PE to mild PE in a pairwise comparison test.
¤P value of comparison among healthy pregnancy, mild PE and severe PE groups.
© Data were expressed as Mean ± SD.
* Data were expressed as Median [IQR].

Table 6
Spearman's rank-order correlations of WBC, ANC, PTC, MPV, PDW, P-LCR and NLR with a MAP in preeclamptic women (n = 63).

Parameters	WBC ($\times 10^3/\mu L$)	ANC ($\times 10^3/\mu L$)	PTC ($\times 10^3/\mu L$)	MPV(fL)	PDW (fL)	P-LCR	NLR
Correlation coefficient (rho)	0.52**	0.51**	−0.33**	0.37**	0.43**	0.44**	0.31**
P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.01

**rho is significant at the 0.01 level (2-tailed).

control group [8,15]. Gosh et al. has similarly reported a higher WBC count in severe PE than the control group, which in line with our study [21]. In addition, the obtained statistically significant higher mean values of WBC and neutrophil count in severe when compared to mild PE, and in mild PE compared to the control group agreed with previous studies [8,21]. In contrast to our finding, no significant differences observed between mild PE and healthy pregnancy in WBC and neutrophil count in the study of Canzoneri et al [8]. There is also evidence that substantiates high activation of leukocytes in maternal circulation and in the placental bed as well during PE [22].

In the present study, ALC was significantly reduced in PE group compared to the control group. The result is in agreement with Alisi P et al. and Lurie et al report [20]. But, the result is different from a study done by Canzoneri et al that they didn't found a statistically significant difference in ALC between PE group and the control group [8]. Evidence suggests that abnormal activation of the immune system may play a role in the aetiology and pathogenesis of PE. The deficiency of regulatory T cell has shown to cause activation of T-helper 1, ultimately the innate immunity. The changes in the innate immunity can also influence the T-helper 1 / regulatory T cell cytokine profile, leading to the activation of peripheral blood granulocytes and deficiency of peripheral blood lymphoid cells [24].

A significant decline of PTC shown in PE compared to the control group is in harmony with the findings of previous studies [14,25]. However, in some studies [6,23], statistically significant difference was not observed between the two groups. In agreement with previous reports [6,25], the value of MPV was significantly higher in PE group compared to the control group. Similarly, PDW and P-LCR were significantly higher in PE group, which is consistent with the result of the previous study [25]. In multiple pairwise comparisons of the current study, the PTC in severe PE was significantly lower when compared to the control group. This result was similar to many previously reported studies [8,26]. While the value of MPV, PDW and P-LCR were significantly higher in severe PE compared to the control group. In agreement with this finding, the earlier study also reported an elevated P-LCR, MPV and PDW [26]. The same study has also reported that reduced PTC, and increased MPV, PDW and P-LCR were found in mild PE group compared with the control group [26]. Thus, these findings have supported our study in which we revealed comparable results. However, Yang et al was not observed significant variations of PTC between severe PE and the control groups [27]. Comparing to mild PE, decreased PTC, and increased MPV, PDW and P-LCR values were seen in severe PE, which is in agreement with previous reports [26,27]. In PE, the lifespan of platelets decrease from 3 to 5 days, and the aggregation and destruction of platelets occur as a result of the altered membrane structure of platelets [28]. These mechanisms could be the possible reason for the observed decrease in PTC among PE group. Endothelial damage and peripheral consumption may also cause thrombocytopenia in PE. The increase in MPV and PDW in mild and severe PE most likely points out increased platelet turn over which could substantiate the evidence that platelet survival time is decreased, resulting in the increased destruction of platelets [26,29]. The elevation of P-LCR levels in PE group could indicate high bone marrow activity [26]. Many studies proposed that activated platelets become larger in size resulting in higher platelet indices; for instance, MPV, PDW and P-LCR [26,29,30].

Endothelial dysfunction and inflammation are essential mechanisms for the establishment and progression of atherosclerosis and PE [30]. As Turkmen et al cited in their study, NLR and PLR were demonstrated in numerous studies as new inflammation markers in cardiac and non-cardiac diseases mediated by the inflammatory process [9]. However, there is no previous reports detailing the role of PLR and NLR in PE. The result from the present study has shown a statistically significant higher NLR level in PE group compared with the control group. This result is consistent with the finding of a previous study done by Oylumlu et al [30], but it is different from the finding of Yavuzcan et al. [15] who found no significant difference between PE group and the control group. The possible reason for the discrepancy might be attributed to the retrospective design that Yavuzcan et al used, as the confounding factors might not be properly controlled in a retrospective design. It is also noticed that NLR has shown a significant rise as the disease advances. As to PLR, significant elevation was noticed in severe PE group compared to the control. However, Yavuzcan et al. [15] were not found a significant difference in the mean value of PLR between severe PE group and the control group. This needs further experimental studies to explore the biological mechanisms how PE influences NLR and PLR.

In this study, it has been observed that WBC, ANC and NLR were significantly correlated with a MAP in PE group. MAP, as an indicator of disease severity, has been significantly and positively correlated with total WBC and ANC, which is nearly similar to Mihu et al. [22] study that reported a significant positive correlation of leukocytes and DBP, and neutrophils and DBP. In platelet parameters analysis, PTC has shown a statistically significant negative correlation, while MPV, PDW and P-LCR have shown positive correlations with a MAP in PE group. Nevertheless, only one study, as far as we know, has been done regarding correlations of platelet parameters with the MAP as an index of disease severity, in which a statistically notable positive correlation has been demonstrated between PDW and MAP [27]. A prospective study, in which DBP was used as diagnostic criteria, revealed a strongest negative correlation between PTC and blood pressure, whereas MPV and PDW were found to be correlated with blood pressure in the positive direction [14].

5.1. Limitation

The major limitation of this study is that it is a single-centre study which can limit its generalizability of the result to the population in the area. Another limitation of this study is that the sample size is not large. This may also limit the statistical power of the study. The cross-sectional nation of the study design does not also establish cause-effect-relationship, so that which appeared first, either PE or hematological parameter changes, remained dilemmatic.

6. Conclusion

In conclusion, the study demonstrates that significantly increased values of total WBC, ANC, NLR, MPV, PDW AMC, and P-LCR; and significantly reduced values of PTC and ALC were found in PE compared to the control group. Moreover, total WBC, ANC, NLR, MPV, PDW and P-LCR were positively correlated with a MAP, whereas PTC was negatively correlated with a MAP in PE group. Hence, monitoring of hematological parameters can be used as clinical indicators in the assessment of severity of PE and may be taken as a useful parameter to prevent complications of PE. However, further multicenter prospective

cohort studies with large sample size are required to verify the role these parameters in the diagnosis of PE and assessment of disease severity.

7. Competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.preghy.2018.06.006.

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